TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED / ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		ATTORNEY'S DOCKET NUMBER P67431US0
		US APPLICATION NO (IF KNOWN, SEE 37 CFR 1.5) 09/926820
INTERNATIONAL APPLICATION NO PCT/EP99/04331	INTERNATIONAL FILING DATE 22 June 1999	PRIORITY DATE CLAIMED 22 June 1999

TITLE OF INVENTION

SERINE PROTEASE INHIBITORS

APPLICANT(S) FOR DO/EO/US

Wolf-Georg FORSSMANN, Hans-Juergen MAEGERT, Ludger STAENDKER and Peter KREUTZMANN

Applicant herein submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for Internatl. Preliminary Examination was made by the 19th month from earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the Internatl. Preliminary Examination report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:
    International Search Report - EPO
    PCT/IB/301 Form
    PCT/IB/308 Form
    First Page of Publication
    International Preliminary Examination Report - with no annexes
    Sequence Listing

531 Rec'd PCT/ 26 DEC 2001

US APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/926820	PCT/EP99/04331	P67431US0

	CALCULATIONS	PTO USE ONLY
17. ☒ The following fees are submitted:		
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Internatl. prelim. examination fee paid to USPTO (37 CFR 1.492 (a) (1)) . . $710.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (2)) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) . . $740.00		
Neither international preliminary examination fee (37 CFR 1.492 (a) (3)) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO) **$1040.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (4)) and all claims satisfied provisions of PCT Article 33(2)-(4) $100.00		
Search Report prepared by the EPO or JPO (37 CFR 1.492 (a) (5)) **$890.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of $130.00 for furnishing the **oath or declaration** later than ☐ **20** ☒ **30** months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130.00	

Claims	**Number Filed**	**Number Extra**	Rate	
Total Claims	**14** - 20 =	-0-	x $18.00	$
Independent Claims	**1** - 3 =	-0-	x $84.00	$
Multiple Dependent Claim(s) (if applicable)			+ $280.00	$
TOTAL OF ABOVE CALCULATIONS =				$ 1020.00
Reduction by 1/2 for filing by **small entity**, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$ 510.00
SUBTOTAL =				$ 510.00
Processing fee of $130 for furnishing the **English translation** later than ☐ **20** ☐ **30** months from the earliest claimed priority date (37 CFR 1.492(f))				$
TOTAL NATIONAL FEE =				$ 510.00
Fee of $40.00 for recording the enclosed **assignment** (37 CFR 1.21(h)). Assignment must be accompanied by appropriate cover sheet (37 CFR 3.28, 3.31).				$
TOTAL FEES ENCLOSED =				$ 510.00
				Amt. to be refunded: $
				Amt. charged: $

a. ☒ A check in the amount of $ 510.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. **06-1358** in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge my account any additional fees set forth in §1.492 during the pendency of this application, or credit any overpayment to Deposit Account No. **06-1358**. A duplicate copy of this sheet is enclosed.

SEND ALL CORRESPONDENCE TO:

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By William E. Player
William E. Player
Reg. No. 31,409
2.7.215

JPH&S 3/99

ATTY. DOCKET NO. P67431US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: FORSSMANN et al.

Serial No.: 09/926,820

Filed: December 26, 2001

For: SERINE PROTEASE INHIBITORS

AMENDMENT

Commissioner of Patents
BOX PCT
Washington, D.C. 20231

Sir:

The instant amendment is submitted in conjunction with the Response to Notice to Comply With Sequence Rules, submitted herewith.

IN THE SPECIFICATION

Replace the originally filed Sequence Listing with the Sequence Listing filed concurrently herewith.

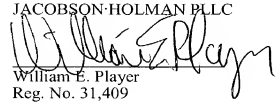
REMARKS

By the instant amendment, the Sequence Listing filed, concurrently herewith, is added to the specification.

Favorable action is requested.

Respectfully submitted,

JACOBSON·HOLMAN PLLC

By: 
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Atty. Dkt. No.: P67431US0
Date: May 6, 2002
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Atty. Dkt. No. P67431US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of Wolf-Georg Forssmann

Serial No.: National Stage of PCT/EP99/04331

Filed: HEREWITH

For: SERINE PROTEASE INHIBITORS

PRELIMINARY AMENDMENT

Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to calculating the filing fee, please amend the captioned application as follows.

IN THE CLAIMS

Cancel claims 1-14, without prejudice or disclaimer.

Add the following claims.

15. A serine protease inhibitor having the amino acid sequence according to SEQ ID NO: 1.

16. A fragment of the serine protease inhibitor having the amino acid sequence

$$R_1\text{-}X\text{-}R_2,$$

wherein R_1 is NH_2, an amino acid or a peptide with up to 100 amino acids, and R_2 is COOH, $CONH_2$, an amino acid or a peptide with up to 100 amino acids, and X is selected from SEQ ID NOS: 2 to 6.

17. A nucleic acid coding for a serine protease inhibitor according to claim 15, especially SEQ ID NOS: 7 to 12.

18. A medicament containing at least one serine protease inhibitor according to claim 15 and/or a nucleic acid coding for the serine protease inhibitor, optionally together with a pharmaceutical vehicle.

19. The medicament according to claim 18, containing from 0.01 to 1000 mg per kg of body weight of the serine protease inhibitor and/or the nucleic acid.

20. Use of the serine protease inhibitor according to claim 15 for preparing a medicament for the treatment of acute or chronic cervix inflammations, inflammations of Bartholin's glands and other vaginal regions, tonsillitis, pharyngitis and laryngitis, acute or chronic inflammatory processes accompanied by excessive formation of mucus and the resulting acute emergency situations, postoperative bleedings due to hyperfibrinolysis, and for the prophylaxis of lung emphysema formation in deficiencies of α_1-proteinase inhibitor.

21. Use of the medicament according to claim 18 for the therapy of asthma, AIDS, pneumonia, tumor diseases and leukemia.

22. Use of the nucleic acid according to claim 17 for preparing a medicament for use in gene therapy for the curing and prophylaxis of acute or chronic cervix inflammations, inflammations of Bartholin's glands and other vaginal regions, tonsillitis, pharyngitis and laryngitis, acute or chronic inflammatory processes accompanied by excessive formation of mucus and the resulting acute emergency situations, postoperative bleedings due to hyperfibrinolysis, and for the prophylaxis of lung emphysema formation in deficiencies of α_1-proteinase inhibitor.

23. Antibodies or antibody fragments against epitopes of the compound according to claim 15.

24. Poly- or oligonucleotides which will hybridize to regions of the cDNA or corresponding RNA under stringent conditions and optionally prevent the expression of coding regions of the genes coding for the compound according to claim 15.

25. A diagnostic agent containing at least one compound according to claim 23.

26. A medicament containing at least one compound according to claim 23 in a therapeutically effective amount.

27. Use of the compound of claim 23 for preparing a medicament for the treatment of diseases involving too high an expression of the serine protease inhibitor or too high an activity of the regions coding for the serine protease inhibitor.

28. DNA coding for the compound of claim 15 and/or RNA involved in the transcription or translation of the compound.

REMARKS

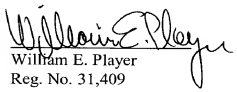
The present claims are 15-28.

The present claims correspond to original claims 1-14, rewritten to eliminate multiple dependencies and to more clearly define the invention.

PCT/EP99/04331
Atty. Dkt. No. P67431US0

Favorable action is requested.

Respectfully submitted,

By: 
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Serine Protease Inhibitors

The present invention relates to serine protease inhibitors, cDNA coding for serine protease inhibitors, medicaments containing such inhibitors or their coding nucleic acid, use of the compounds according to the invention for the preparation of medicaments for the treatment of various indications, antibodies or antibody fragments against epitopes of the compounds according to the invention, poly- or oligonucleotides which will hybridize to genes of the compounds according to the invention, a diagnostic agent for detecting the compounds according to the invention, and medicaments containing antibodies or poly- or oligonucleotides according to the invention.

Proteolytic processes play an important physiological role in all organisms; a distinction has to be made between non-specific and specific proteolytic reactions. The former include, for example, the digestion of food in the digestive tract by endopeptidases, and the intracellular degradation of used endogenous substances and phagocytosed materials by lysosomal proteases. Specific proteolyses mostly serve for the conversion of a proenzyme to its active form, as in the conversion of trypsinogen to trypsin, and of chymotrypsinogen to chymotrypsin, and in the callicrein-kinin cascades and the blood clotting cascade. Depending on the structure of the reactive site of the proteinases involved, they are classified into the classes of serine proteases (e.g., chymotrypsin, trypsin, elastase and cathepsin G), aspartate proteases (e.g., cathepsin D, cathepsin E and pepsin), cysteine proteases (e.g., cathepsin B, cathepsin H and cathepsin L), and the metallo-proteases (e.g., collagenase and thermolysin).

In order to be able to correct the proteolytic processes which often proceed in a cascade, the organisms is provided with a number of other proteins, the protease inhibitors (for a survey, see Laskowski and Kato, 1980, and Bode and

Huber, 1992). Thus, the liver-synthesized human plasma protease inhibitors α_1-antichymotrypsin and α_1-proteinase inhibitors protect the lung tissue from non-specific attack by the proteinases cathepsin G and elastase from polymorphonuclear lymphocytes. When the balance between proteases and their specific inhibitors is disturbed, pathological effects may arise. For example, an excess ratio of elastase to α_1-proteinase inhibitor increases the risk of formation of a lung emphysema by a factor of about 20 to 30 in patients with a genetically caused deficiency in this factor as compared to the normal population (Carrel and Owen, 1980). With smokers, the formation of an emphysema is promoted by oxidation of the amino acid methionine which is present in the reactive site of the α_1-proteinase inhibitor by oxidants contained in cigarette smoke (Miller and Kuschner, 1969; Ohlsson et al., 1980). Also in the case of infection with Gram-negative bacteria, their endotoxins can cause disintegration of phagocytes and thus the secretion of lysosomal proteases, which may cause an uncontrolled damage to tissues and inflammations due to the increased consumption of protease inhibitors. For this reason, certain protease inhibitors have a high therapeutic potential (see, e.g., Fritz, 1980).

International Application PCT/EP 98/08424 relates to serine protease inhibitors, wherein said serine protease inhibitors have a domain with four cysteines, and a sequence of from 0 to 20 amino acids is present between the first and second cysteines, or said serine protease inhibitors have a domain of six cysteines, and a sequence of from 7 to 20 amino acids is present between the first and second cysteines.

It has been the object of the present invention to provide further serine protease inhibitors.

This object is achieved by a serine protease inhibitor having the amino acid sequence according to SEQ ID NO: 1.

The present invention also relates to fragments of the serine protease inhibitor according to the invention having the amino acid sequence R_1-X-R_2, wherein R_1 is NH_2, an amino acid or a peptide with up to 100 amino acids, and R_2 is COOH, $CONH_2$, an amino acid or a peptide with up to 100 amino acids, and X is selected from SEQ ID NOS: 2 to 6.

It is preferred that the serine protease inhibitor contains one or more disulfide bridges. It is particularly preferred for it to contain a disulfide bridge between the first and fourth cysteines and/or between the second and third cysteines, or to contain a disulfide bridge between the first and fifth cysteines and/or between the second and fourth cysteines and/or between the third and sixth cysteines.

In addition to the amino acid sequence of the preferred compounds according to the invention, further information about the cDNA coding for the compounds according to the invention can also be seen from Figure 1. In particular, the corresponding motifs and primer-hybridizing sites are indicated.

According to the invention, nucleic acids coding for the compounds according to the invention, especially a DNA having the nucleic acid sequence according to SEQ ID NOS: 7 to 12, are also claimed.

The compounds according to the invention are useful as medicaments. In this case, they are administered together with pharmaceutically acceptable vehicles.

The medicaments according to the invention containing the protease inhibitors according to the invention are preferably administered in amounts of from 1 to 100 mg/kg of the patient's body weight. As the dosage form, all galenic formulations for peptide active substances may be used. The medicaments containing nucleic acids according to the invention are preferably administered in amounts of from 0.1 to 100 mg/kg of body weight of a corresponding patient. In this case, the galenic dosage forms which may be used are those which are suitable for the administration of nucleic acids without rendering the nucleic

acids ineffective by metabolic influences before they have reached their site of action. For example, liposomes in which the nucleic acids are contained can be employed as a galenic dosage form.

The compounds according to the invention can be used, in particular, for the treatment of acute or chronic cervix inflammations, inflammations of Bartholin's gland or other vaginal regions, tonsillitis, pharyngitis and laryngitis, acute or chronic inflammatory processes accompanied by excessive formation of mucus and the resulting acute emergency situations, postoperative bleedings due to hyperfibrinolysis, and for the prophylaxis of lung emphysema formation in deficiencies of α_1-proteinase inhibitor.

Further, they may be employed for the therapy of asthma, AIDS, tumor diseases and leukemia.

The compounds according to the invention can be administered in deficiencies of serine protease inhibitors to correct endogenous defects. The nucleic acids may also be used in gene therapy, either directly or coupled to suitable vehicles. Suitable vectors include, in particular, attenuated adenoviruses into which the corresponding genes have been incorporated.

The polypeptides according to the invention can serve for the preparation of antibodies or antibody fragments. These are simply prepared by the immunization of appropriate mammals. By per se known operations, the antibodies may also be humanized so that such antibodies can also be employed for therapeutic use. Antibodies or antibody fragments can then by employed for the regulation of diseases in which the protease inhibitors are expressed in a pathological way. Also, antisense nucleic acids complementary to the nucleic acids according to the invention may be employed in therapeutical use in overexpressions of the protease inhibitor genes.

The compounds according to the invention can be easily prepared by per se known methods of peptide or nucleotide synthesis. Preparation of the compounds by genetic engineering is also possible.

Those skilled in the art will recognize that fragments of the polypeptides according to the invention may also be used provided that they retain the inhibitory properties of the serine protease inhibitors. Those skilled in the art know how to find such fragments. Thus, this may be accomplished, for example, by a selected enzymatic cleavage of the compounds according to the invention. Side-chain modified amino acids may also be employed. N- or C-terminally modified polypeptides may also be used. In particular, phosphorylated, glycosylated, methylated, acetylated or similarly modified polypeptides can be employed provided that they do not substantially affect the activity of the serine protease inhibitors.

Derivatives of the nucleic acids according to the invention which have modified triplet structures in accordance with codon usage may also be used. In addition, nucleic acids according to the invention also include those which are more stable towards degradation by nucleases as compared with the native compounds, for example, the corresponding SODN derivatives usually employed in antisense technology to give the antisense structures a more stable design towards enzymatic attack.

Structures homologous to the polypeptides may also be used. In particular, these include polypeptide structures in which amino acids have been exchanged. Thus, for example, conservative amino acid substitutions in highly conserved regions can be considered as follows: any isoleucine, valine and leucine amino acid can be exchanged for any other of these amino acids, aspartate can be exchanged for glutamate and vice versa, glutamine for asparagine and vice versa, serine for threonine and vice versa. Conservative amino acid substitutions in less highly conserved regions can be as follows: Any of the amino acids isoleucine, valine and leucine for any other of these amino acids, aspartate for

glutamate and vice versa, glutamine for asparagine and vice versa, serine for threonine and vice versa, glycine for alanine and vice versa, alanine for valine and vice versa, any of the amino acids leucine, isoleucine or valine for methionine, lysine for arginine and vice versa, either of the amino acids arginine or lysine for either of the amino acids aspartate or glutamate, either of the amino acids arginine or lysine for histidine, glutamine for glutamate and vice versa, and asparagine for aspartate and vice versa.

CLAIMS:

1. A serine protease inhibitor having the amino acid sequence according to SEQ ID NO: 1.

2. A fragments of the serine protease inhibitor having the amino acid sequence

$$R_1\text{-}X\text{-}R_2,$$

wherein R_1 is NH_2, an amino acid or a peptide with up to 100 amino acids, and R_2 is COOH, $CONH_2$, an amino acid or a peptide with up to 100 amino acids, and X is selected from SEQ ID NOS: 2 to 6.

3. A nucleic acid coding for a serine protease inhibitor according to either of claims 1 or 2, especially SEQ ID NOS: 7 to 12.

4. A medicament containing at least one serine protease inhibitor according to claim 1 or 2 and/or a nucleic acid according to claim 3, optionally together with pharmaceutical vehicles.

5. The medicament according to claim 4, containing from 0.01 to 1000 mg per kg of body weight of the serine protease inhibitor according to claim 1 or 2 and/or of the nucleic acid according to claim 3.

6. Use of the medicament according to claim 1 or 2 for preparing a medicament for the treatment of acute or chronic cervix inflammations, inflammations of Bartholin's glands and other vaginal regions, tonsillitis, pharyngitis and laryngitis, acute or chronic inflammatory processes accompanied by excessive formation of mucus and the resulting acute emergency situations, postoperative bleedings due to hyperfibrinolysis,

and for the prophylaxis of lung emphysema formation in deficiencies of α_1-proteinase inhibitor.

7. Use of the medicament according to claim 4 for the therapy of asthma, AIDS, pneumonia, tumor diseases and leukemia.

8. Use of the nucleic acids according to claim 3 for preparing a medicament for use in gene therapy for the curing and prophylaxis of diseases as mentioned in claim 6.

9. Antibodies or antibody fragments against epitopes of the compounds according to either of claims 1 or 2.

10. Poly- or oligonucleotides which will hybridize to regions of the cDNA or corresponding RNA under stringent conditions and optionally prevent the expression of coding regions of the genes coding for the compounds according to claims 1 or 2 (antisense compounds).

11. A diagnostic agent containing at least one of the compounds according to claim 9 or 10.

12. A medicament containing at least one of the compounds mentioned in claims 9 and/or 10 in therapeutically effective amounts.

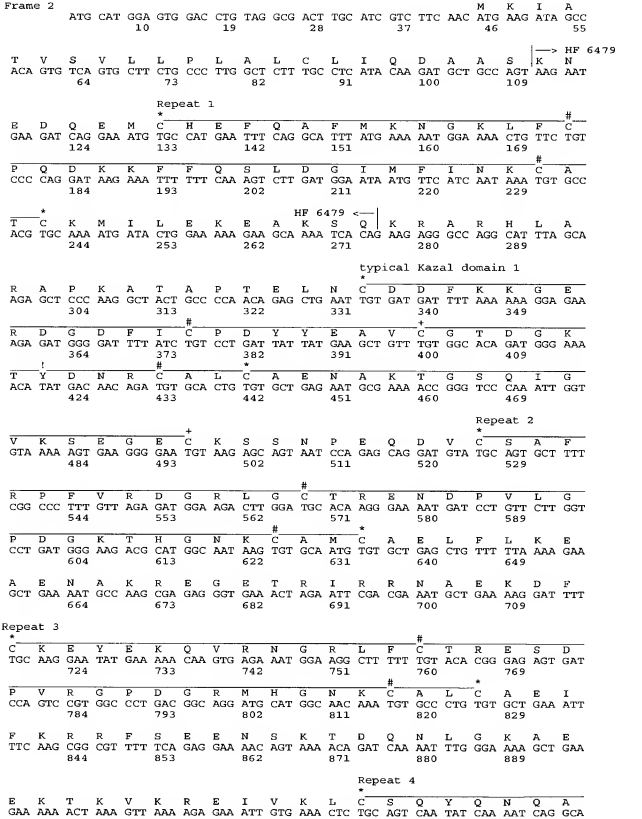
13. Use of the compounds according to claims 9 and/or 10 for preparing a medicament for the treatment of diseases involving too high an expression of the compounds according to claim 1 or 2, or too high an activity of the regions coding for the compounds according to claim 1 or 2.

14. DNA, coding for the compounds mentioned in claim 1 or 2, and/or RNA involved in the transcription or translation of the compounds mentioned in claim 1 or 2.

Abstract

The invention relates to serine protease inhibitors having the amino acid sequence in accordance with Seq. ID No. 1.

Figure 1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Repeat 2
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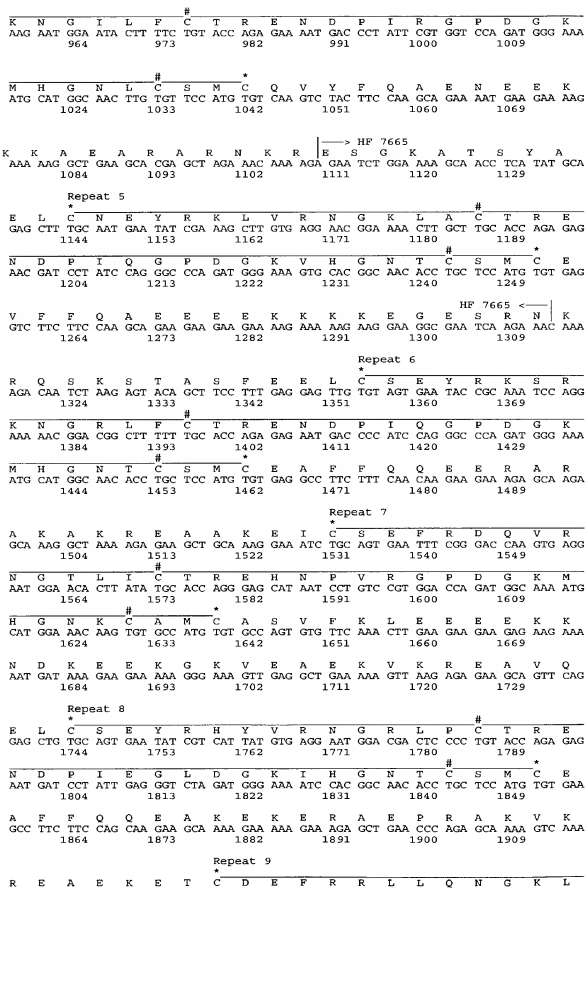
Repeat 4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M H G N L C S M C Q V Y F Q A E N E E K
ATG CAT GGC AAC TTG TGT TCC ATG TGT CAA GTC TAC TTC CAA GCA GAA AAT GAA GAA AAG
1024 1033 1042 1051 1060 1069
HF 7665
K K A E A R A R N K R E S Q K A T S Y A
AAA AAG GCT GAA GCA CGA GCT AGA AAC AAA AGA GAA TCT GGA AAA GCA ACC TCA TAT GCA
1084 1093 1102 1111 1120 1129
Repeat 5
E L C N E Y R K L V R N G K L A C T R E
GAG CTT TGC AAT GAA TAT CGA AAG CTT GTG AGG AAC GGA AAA CTT GCT TGC ACC AGA GAG
1144 1153 1162 1171 1180 1189
N D P I Q G P D G K V H G N T C S M C E
AAC GAT CCT ATC CAG GGC CCA GAT GGG AAA GTG CAC GGC AAC ACC TGC TCC ATG TGT GAG
1204 1213 1222 1231 1240 1249
HF 7665
V F F Q A E E E E K K K K E G E S R N K
GTC TTC TTC CAA GCA GAA GAA GAA GAA AAG AAA AAG AAG GAA GGC GAA TCA AGA AAC AAA
1264 1273 1282 1291 1300 1309
Repeat 6
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1324 1333 1342 1351 1360 1369
K N G R L F C T R E N D P I Q G P D G K
AAA AAC GGA CGG CTT TTT TGC ACC AGA GAG AAT GAC CCC ATC CAG GGC CCA GAT GGG AAA
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1444 1453 1462 1471 1480 1489
Repeat 7
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1624 1633 1642 1651 1660 1669
N D K E E K G K V E A E K V K R E A V Q
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N D P I E G L D G K I H G N T C S M C E
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1804 1813 1822 1831 1840 1849
A F F Q Q E A K E K E R A E P R A K V K
GCC TTC TTC CAG CAA GAA GCA AAA GAA AAA GAA AGA GCT GAA CCC AGA GCA AAA GTC AAA
1864 1873 1882 1891 1900 1909
Repeat 9
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        1924            1933            1942            1951            1960            1969

#
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TTC TGC ACA AGA GAA AAT GAT CCT GTG CGT GGC CCA GAT GGC AAG ACC CAT GGC AAC AAG
        1984            1993            2002            2011            2020            2029

#       *
C   A   M   C   K   A   V   F   Q   K   E   N   E   E   R   K   R   K   E   E
TGT GCC ATG TGT AAG GCA GTC TTC CAG AAA GAA AAT GAG GAA AGA AAG AGG AAA GAA GAG
        2044            2053            2062            2071            2080            2089


E   D   Q   R   N   A   A   G   H   G   S   S   G   G   G   G   G   N   T   Q
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        2104            2113            2122            2131            2140            2149

        Repeat 10
        *                                                                       #
D   E   C   A   E   Y   Q   E   Q   M   K   N   G   R   L   S   C   T   R   E
GAC GAA TGT GCT GAG TAT CAG GAA CAA ATG AAA AAT GGA AGA CTC AGC TGT ACT CGG GAG
        2164            2173            2182            2191            2200            2209

                                                                        #       *
S   D   P   V   R   D   A   D   G   K   S   Y   N   N   Q   C   T   M   C   K
AGT GAT CCT GTA CGT GAT GCT GAT GGC AAA TCG TAC AAC AAT CAG TGT ACC ATG TGT AAA
        2224            2233            2242            2251            2260            2269

A   K   L   E   R   E   A   E   R   K   N   E   Y   S   R   S   R   S   N   G
GCA AAA TTG GAA AGA GAA GCA GAG AGA AAA AAT GAG TAT TCT CGC TCC AGA TCA AAT GGG
        2284            2293            2302            2311            2320            2329

                                                Repeat 11
                                                *
T   G   S   E   S   G   K   D   T   C   D   E   F   R   S   Q   M   K   N   G
ACT GGA TCA GAA TCA GGG AAG GAT ACA TGT GAT GAG TTT AGA AGC CAA ATG AAA AAT GGA
        2344            2353            2362            2371            2380            2389

        #
K   L   I   C   T   R   E   S   D   P   V   R   G   P   D   G   K   T   H   G
AAA CTT ATC TGC ACT CGA GAA AGT GAC CCT GTC CGG GGT CCA GAT GGC AAG ACA CAT GGT
        2404            2413            2422            2431            2440            2449

        #               *
N   K   C   T   M   C   K   E   K   L   E   R   E   A   A   E   K   K   K   K
AAT AAG TGT ACT ATG TGT AAG GAA AAA CTG GAA AGG GAA GCA GCT GAA AAA AAA AAG AAA
        2464            2473            2482            2491            2500            2509

E   D   E   D   R   S   N   T   G   E   R   S   N   T   G   E   R   S   N   D
GAG GAT GAA GAC AGG AGC AAT ACA GGA GAA AGG AGC AAT ACA GGA GAA AGG AGC AAT GAC
        2524            2533            2542            2551            2560            2569

                Repeat 12
                *                                                               #
K   E   D   L   C   R   E   F   R   S   M   Q   R   N   G   K   L   I   C   T
AAA GAG GAT CTG TGT CGT GAA TTT CGA AGC ATG CAG AGA AAT GGA AAG CTT ATC TGC ACC
        2584            2593            2602            2611            2620            2629

                                                                        #
R   E   N   N   P   V   R   G   P   Y   G   K   M   H   I   N   K   C   A   M
AGA GAA AAT AAC CCT GTT CGA GGC CCA TAT GGC AAG ATG CAC ATC AAT AAA TGT GCT ATG
        2644            2653            2662            2671            2680            2689

*
C   Q   S   I   F   D   R   E   A   N   E   R   K   K   K   D   E   E   K   S
TGT CAG AGC ATC TTT GAT CGA GAA GCT AAT GAA AGA AAA AAG AAA GAT GAA GAG AAA TCA
        2704            2713            2722            2731            2740            2749

                                                        Repeat 13
                                                        *
S   S   K   P   S   N   N   A   K   D   E   C   S   E   F   R   N   Y   I   R
AGT AGC AAG CCC TCA AAT AAT GCA AAG GAT GAG TGC AGT GAA TTT CGA AAC TAT ATA AGG
        2764            2773            2782            2791            2800            2809

        #
N   N   E   L   I   C   P   R   E   N   D   P   V   H   G   A   D   G   K   F
AAC AAT GAA CTC ATC TGC CCT AGA GAG AAT GAC CCA GTG CAC GGT GCT GAT GGA AAG TTC
        2824            2833            2842            2851            2860            2869

                #               *
Y   T   N   K   C   Y   M   C   R   A   V   F   L   T   E   A   L   E   R   A
TAT ACA AAC AAG TGC TAC ATG TGC AGA GCT GTC TTT CTA ACA GAA GCT TTG GAA AGG GCA
        2884            2893            2902            2911            2920            2929

K   L   Q   E   K   P   S   H   V   R   A   S   Q   E   E   D   S   P   D   S
AAG CTT CAA GAA AAG CCA TCC CAT GTT AGA GCT TCT CAA GAG GAA GAC AGC CCA GAC TCT
        2944            2953            2962            2971            2980            2989
```

typical Kazal domain 2

```
                                        *
F   S   S   L   D   S   E   M   C   K   D   Y   R   V   L   P   R   I   G   Y
TTC AGT TCT CTG GAT TCT GAG ATG TGC AAA GAC TAC CGA GTA TTG CCC AGG ATA GGC TAT
        3004            3013            3022            3031            3040            3049
    #                                   +                                       !
L   C   P   K   D   L   K   P   V   C   G   D   D   G   Q   T   Y   N   N   P
CTT TGT CCA AAG GAT TTA AAG CCT GTC TGT GGT GAC GAT GGC CAA ACC TAC AAC AAT CCT
        3064            3073            3082            3091            3100            3109
#                   *
C   M   L   C   H   E   N   L   I   R   Q   T   N   T   H   I   R   S   T   G
TGC ATG CTC TGT CAT GAA AAC CTG ATA CGC CAA ACA AAT ACA CAC ATC CGC AGT ACA GGG
        3124            3133            3142            3151            3160            3169
    +
K   C   E   E   S   S   T   P   G   T   T   A   A   S   M   P   P   S   D   E
AAG TGT GAG GAG AGC AGC ACC CCA GGA ACC ACC GCA GCC AGC ATG CCC CCG TCT GAC GAA
        3184            3193            3202            3211            3220            3229


TGA CAG GAA GAT TGT TGA AAG CCA TGA GGG AAA AAA TAA ACC CCA GTT CTG AAT CAC CTA
        3244            3253            3262            3271            3280            3289


CCT TCA CCA TCT GTA TAT ACA AAG AAT TCT TCG GAG CTT GTC TTA TTT GCT ATA GAA AAC
        3304            3313            3322            3331            3340            3349


AAT ACA GAG CTT TTG GGA ATG GAA TCA CTG ATT TTC AGT CTT TTC CAT TTC TTT CCT CCT
        3364            3373            3382            3391            3400            3409


AGA ATC TGT GAT CTG AGG GTA TAA AGA CAT TTC CAC CAA GTT TGA GCC CTC AAA ATG TCC
        3424            3433            3442            3451            3460            3469

                                    polyadenylation signal
TGA TTA CAA TGC TGT CTG TCC AAC TGC CTG TTC AAT AAA AGT AAA CTC AGC AGA AAA....
        3484            3493            3502            3511            3520            3529


.......poly(A) tail
```

The following sequence corrections have been performed:

An additional A in position 2510 results in a frame shift which produces three additional inhibitor domains.

Base were exchanged in ten different positions:

Position 551: G for A
Position 1207: C for T
Position 1258: C for T
Position 1261: C for T
Position 2175: A for G
Position 2950: G for A
Position 3228: C for T
Position 3284: C for T
Position 3324: C for T
Position 3337: C for T

SEQUENZPROTOKOLL

<110> Forssmann Prof., Wolf-Georg

<120> Serin-Proteinase-Inhibitoren

<130> Forssmann

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<141>

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<170> PatentIn Ver. 2.1

<210> 1

DECLARATION AND POWER OF ATTORNEY U.S.A.

FOR ATTORNEYS' USE ONLY

ATTORNEYS' DOCKET NO.

ALL PATENTS, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT, PARIS CONVENTION,
NON PRIORITY, OR PROVISIONAL APPLICATIONS

As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled

101 / 102 Serine Protease Inhibitors

which is described and claimed in:

☒ PCT International Application No. PCT/EP99/04331 filed June 22, 1999

☐ the attached specification

☐ the specification in application Serial No. _____ filed _____

(if applicable) and amended on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

(Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed Yes	No
			☐	☐
			☐	☐
			☐	☐

103 / 104

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing Date)	(Status: patented, pending, abandoned)

(10)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys (Registration No.) to prosecute this application, receive and act on instructions from my agent, and transact all business in the Patent and Trademark Office connected therewith. HARVEY B. JACOBSON, JR. (20,851), JOHN CLARKE HOLMAN (22,769), MARVIN R. STERN (20,640), ALLEN S. MELSER (27,215); MICHAEL R. SLOBASKY (26,421); JONATHAN L. SCHERER (29,851); IRWIN M. AISENBERG (19,007), WILLIAM E. PLAYER (31,409); YOON S. HAM (45,307) and NATHANIEL A. HUMPHRIES (22,772)

SEND CORRESPONDENCE TO CUSTOMER NO. 00136 or **JACOBSON HOLMAN** PROFESSIONAL LIMITED LIABILITY COMPANY 400 SEVENTH STREET, N.W. WASHINGTON, D.C. 20004	DIRECT TELEPHONE CALLS TO. (please use Attorney's Docket No.) (202) 638-6666 **JACOBSON HOLMAN** PROFESSIONAL LIMITED LIABILITY COMPANY

*Inventor(s) name must include at least one unabbreviated first or middle name.

1-00

201	FULL NAME * OF INVENTOR	FAMILY NAME Forssmann	GIVEN NAME Wolf-Georg	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY Hannover DEX	STATE OR FOREIGN COUNTRY Germany	COUNTRY OF CITIZENSHIP Germany	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS Blücherstr. 5	CITY Hannover	STATE OR COUNTRY Germany	ZIP CODE 30175
2-00	FULL NAME * OF INVENTOR	FAMILY NAME Mägert	GIVEN NAME Hans-Jürgen	MIDDLE NAME	
202	RESIDENCE & CITIZENSHIP	CITY Hannover DEX	STATE OR FOREIGN COUNTRY Germany	COUNTRY OF CITIZENSHIP Germany	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS Moltkeplatz 8	CITY Hannover	STATE OR COUNTRY Germany	ZIP CODE 30163
3-00	FULL NAME * OF INVENTOR	FAMILY NAME Ständker	GIVEN NAME Ludger	MIDDLE NAME	
203	RESIDENCE & CITIZENSHIP	CITY Hannover DEX	STATE OR FOREIGN COUNTRY Germany	COUNTRY OF CITIZENSHIP Germany	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS Dohmeyers Weg 25	CITY Hannover	STATE OR COUNTRY Germany	ZIP CODE 30625

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201*	SIGNATURE OF INVENTOR 202*	SIGNATURE OF INVENTOR 203*
DATE 12/13/2001	DATE 13.12.2001	DATE 13.12.2001

☐ Additional inventors are named on separately numbered sheets attached hereto.

FOR ATTORNEYS' USE ONLY

ATTORNEYS' DOCKET NO.

DECLARATION AND POWER OF ATTORNEY U.S.A.

* ALL PATENTS, INCLUDING DESIGN
* FOR APPLICATION BASED ON PCT; PARIS CONVENTION; NON PRIORITY; OR PROVISIONAL APPLICATIONS

As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled:

101 Serine Protease Inhibitors

102 which is described and claimed in:

☒ PCT International Application No. PCT/EP99/04331 filed June 22, 1999

☐ the attached specification ☐ the specification in application Serial No. _____ filed _____

(if applicable) and amended on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
103 (Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
104 (Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No

I hereby claim the benefit under Title 35, United States Code,§119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105 I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) (Status: patented, pending, abandoned)

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SEND CORRESPONDENCE TO: **CUSTOMER NO. 00136**
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*Inventor(s) name must include at least one unabbreviated first or middle name.

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201	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
		Kreutzmann	Peter		
		Magdeburg DEX	Germany	Germany	
		Rautenbreite 11	Magdeburg	Germany	39116
202	FULL NAME * OF INVENTOR	FAMILY NAME	GIVEN NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
203	FULL NAME * OF INVENTOR	FAMILY NAME	GIVEN NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201*	SIGNATURE OF INVENTOR 202*	SIGNATURE OF INVENTOR 203*
Peter Kreutzmann		
DATE 13.12.2001	DATE	DATE

☐ Additional inventors are named on separately numbered sheets attached hereto.

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MAGERT, HANS-JURGEN
STANDKER, LUDGER
KREUTZMANN, PETER

<120> SERINE PROTEASE INHIBITORS

<130> 10496-P67431US0

<140> 09/926,820
<141> 2001-12-26

<150> PCT/EP99/04331
<151> 1999-06-22

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<170> PatentIn Ver. 2.1

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            20                  25                  30

Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys
        35                  40                  45

Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala
    50                  55                  60

Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala
65                  70                  75                  80

Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn
                85                  90                  95

Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro
            100                 105                 110

Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn
        115                 120                 125

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    130                 135                 140

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                165                 170                 175

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            180                 185                 190

Lys Cys Ala Met Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala
        195                 200                 205

Lys Arg Glu Gly Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe
    210                 215                 220

Cys Lys Glu Tyr Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr
225                 230                 235                 240

Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn
                245                 250                 255

Lys Cys Ala Leu Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu
            260                 265                 270

Asn Ser Lys Thr Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys
        275                 280                 285

Val Lys Arg Glu Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala
    290                 295                 300

Lys Asn Gly Ile Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly
305                 310                 315                 320

Pro Asp Gly Lys Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr
                325                 330                 335

Phe Gln Ala Glu Asn Glu Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg
            340                 345                 350

Asn Lys Arg Glu Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn
        355                 360                 365

Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu
    370                 375                 380

Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys
385                 390                 395                 400

Ser Met Cys Glu Val Phe Phe Gln Ala Glu Glu Glu Glu Lys Lys Lys
                405                 410                 415

Lys Glu Gly Glu Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser
            420                 425                 430

Phe Glu Glu Leu Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg
        435                 440                 445

Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys
    450                 455                 460
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Glu Arg Ala Arg Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys
                485                 490                 495

Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg
            500                 505                 510

Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys
        515                 520                 525

Cys Ala Met Cys Ala Ser Val Phe Lys Leu Glu Glu Glu Glu Lys Lys
    530                 535                 540

Asn Asp Lys Glu Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg
545                 550                 555                 560

Glu Ala Val Gln Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn
                565                 570                 575

Gly Arg Leu Pro Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp
            580                 585                 590

Gly Lys Ile His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln
        595                 600                 605

Gln Glu Ala Lys Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys
    610                 615                 620

Arg Glu Ala Glu Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln
625                 630                 635                 640

Asn Gly Lys Leu Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro
                645                 650                 655

Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe
            660                 665                 670

Gln Lys Glu Asn Glu Glu Arg Lys Arg Lys Glu Glu Glu Asp Gln Arg
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Asp Glu Cys Ala Glu Tyr Gln Glu Gln Met Lys Asn Gly Arg Leu Ser
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tatgcatgga gtggacctgt aggcgacttg catcgtcttc aac atg aag ata gcc   55
                                                Met Lys Ile Ala
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aca gtg tca gtg ctt ctg ccc ttg gct ctt tgc ctc ata caa gat gct   103
Thr Val Ser Val Leu Leu Pro Leu Ala Leu Cys Leu Ile Gln Asp Ala
  5                  10                  15                  20

gcc agt aag aat gaa gat cag gaa atg tgc cat gaa ttt cag gca ttt   151
Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu Phe Gln Ala Phe
                25                  30                  35

atg aaa aat gga aaa ctg ttc tgt ccc cag gat aag aaa ttt ttt caa   199
Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys Lys Phe Phe Gln
            40                  45                  50

agt ctt gat gga ata atg ttc atc aat aaa tgt gcc acg tgc aaa atg   247
Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala Thr Cys Lys Met
        55                  60                  65
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ata ctg gaa aaa gaa gca aaa tca cag aag agg gcc agg cat tta gca   295
Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala Arg His Leu Ala
      70                  75                  80

aga gct ccc aag gct act gcc cca aca gag ctg aat tgt gat gat ttt   343
Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn Cys Asp Asp Phe
 85                  90                  95                 100

aaa aaa gga gaa aga gat ggg gat ttt atc tgt cct gat tat tat gaa   391
Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro Asp Tyr Tyr Glu
                105                 110                 115

gct gtt tgt ggc aca gat ggg aaa aca tat gac aac aga tgt gca ctg   439
Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn Arg Cys Ala Leu
            120                 125                 130

tgt gct gag aat gcg aaa acc ggg tcc caa att ggt gta aaa agt gaa   487
Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly Val Lys Ser Glu
        135                 140                 145

ggg gaa tgt aag agc agt aat cca gag cag gat gta tgc agt gct ttt   535
Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Asp Val Cys Ser Ala Phe
    150                 155                 160

cgg ccc ttt gtt aga gat gga aga ctt gga tgc aca agg gaa aat gat   583
Arg Pro Phe Val Arg Asp Gly Arg Leu Gly Cys Thr Arg Glu Asn Asp
165                 170                 175                 180

cct gtt ctt ggt cct gat ggg aag acg cat ggc aat aag tgt gca atg   631
Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met
                185                 190                 195

tgt gct gag ctg ttt tta aaa gaa gct gaa aat gcc aag cga gag ggt   679
Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala Lys Arg Glu Gly
            200                 205                 210

gaa act aga att cga cga aat gct gaa aag gat ttt tgc aag gaa tat   727
Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe Cys Lys Glu Tyr
        215                 220                 225

gaa aaa caa gtg aga aat gga agg ctt ttt tgt aca cgg gag agt gat   775
Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr Arg Glu Ser Asp
    230                 235                 240

cca gtc cgt ggc cct gac ggc agg atg cat ggc aac aaa tgt gcc ctg   823
Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn Lys Cys Ala Leu
245                 250                 255                 260

tgt gct gaa att ttc aag cgg cgt ttt tca gag gaa aac agt aaa aca   871
Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu Asn Ser Lys Thr
                265                 270                 275

gat caa aat ttg gga aaa gct gaa gaa aaa act aaa gtt aaa aga gaa   919
Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys Val Lys Arg Glu
            280                 285                 290
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att gtg aaa ctc tgc agt caa tat caa aat cag gca aag aat gga ata   967
Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala Lys Asn Gly Ile
        295                 300                 305

ctt ttc tgt acc aga gaa aat gac cct att cgt ggt cca gat ggg aaa  1015
Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly Pro Asp Gly Lys
    310                 315                 320

atg cat ggc aac ttg tgt tcc atg tgt caa gtc tac ttc caa gca gaa  1063
Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr Phe Gln Ala Glu
325                 330                 335                 340

aat gaa gaa aag aaa aag gct gaa gca cga gct aga aac aaa aga gaa  1111
Asn Glu Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg Asn Lys Arg Glu
                345                 350                 355

tct gga aaa gca acc tca tat gca gag ctt tgc aat gaa tat cga aag  1159
Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn Glu Tyr Arg Lys
            360                 365                 370

ctt gtg agg aac gga aaa ctt gct tgc acc aga gag aac gat cct atc  1207
Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu Asn Asp Pro Ile
        375                 380                 385

cag ggc cca gat ggg aaa gtg cac ggc aac acc tgc tcc atg tgt gag  1255
Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys Ser Met Cys Glu
    390                 395                 400

gtc ttc ttc caa gca gaa gaa gaa gaa aag aaa aag aag gaa ggc gaa  1303
Val Phe Phe Gln Ala Glu Glu Glu Glu Lys Lys Lys Lys Glu Gly Glu
405                 410                 415                 420

tca aga aac aaa aga caa tct aag agt aca gct tcc ttt gag gag ttg  1351
Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser Phe Glu Glu Leu
                425                 430                 435

tgt agt gaa tac cgc aaa tcc agg aaa aac gga cgg ctt ttt tgc acc  1399
Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg Leu Phe Cys Thr
            440                 445                 450

aga gag aat gac ccc atc cag ggc cca gat ggg aaa atg cat ggc aac  1447
Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Met His Gly Asn
        455                 460                 465

acc tgc tcc atg tgt gag gcc ttc ttt caa caa gaa gaa aga gca aga  1495
Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Gln Glu Glu Arg Ala Arg
    470                 475                 480

gca aag gct aaa aga gaa gct gca aag gaa atc tgc agt gaa ttt cgg  1543
Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys Ser Glu Phe Arg
485                 490                 495                 500

gac caa gtg agg aat gga aca ctt ata tgc acc agg gag cat aat cct  1591
Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg Glu His Asn Pro
                505                 510                 515
```

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gtc cgt gga cca gat ggc aaa atg cat gga aac aag tgt gcc atg tgt   1639
Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys Cys Ala Met Cys
            520                 525                 530

gcc agt gtg ttc aaa ctt gaa gaa gaa gag aag aaa aat gat aaa gaa   1687
Ala Ser Val Phe Lys Leu Glu Glu Glu Glu Lys Lys Asn Asp Lys Glu
        535                 540                 545

gaa aaa ggg aaa gtt gag gct gaa aaa gtt aag aga gaa gca gtt cag   1735
Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg Glu Ala Val Gln
    550                 555                 560

gag ctg tgc agt gaa tat cgt cat tat gtg agg aat gga cga ctc ccc   1783
Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn Gly Arg Leu Pro
565                 570                 575                 580

tgt acc aga gag aat gat cct att gag ggt cta gat ggg aaa atc cac   1831
Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp Gly Lys Ile His
                585                 590                 595

ggc aac acc tgc tcc atg tgt gaa gcc ttc ttc cag caa gaa gca aaa   1879
Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Gln Glu Ala Lys
            600                 605                 610

gaa aaa gaa aga gct gaa ccc aga gca aaa gtc aaa aga gaa gct gaa   1927
Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys Arg Glu Ala Glu
        615                 620                 625

aag gag aca tgc gat gaa ttt cgg aga ctt ttg caa aat gga aaa ctt   1975
Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln Asn Gly Lys Leu
    630                 635                 640

ttc tgc aca aga gaa aat gat cct gtg cgt ggc cca gat ggc aag acc   2023
Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro Asp Gly Lys Thr
645                 650                 655                 660

cat ggc aac aag tgt gcc atg tgt aag gca gtc ttc cag aaa gaa aat   2071
His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe Gln Lys Glu Asn
                665                 670                 675

gag gaa aga aag agg aaa gaa gag gaa gat cag aga aat gct gca gga   2119
Glu Glu Arg Lys Arg Lys Glu Glu Glu Asp Gln Arg Asn Ala Ala Gly
            680                 685                 690

cat ggt tcc agt ggt ggt gga gga gga aac act cag gac gaa tgt gct   2167
His Gly Ser Ser Gly Gly Gly Gly Gly Asn Thr Gln Asp Glu Cys Ala
        695                 700                 705

gag tat cag gaa caa atg aaa aat gga aga ctc agc tgt act cgg gag   2215
Glu Tyr Gln Glu Gln Met Lys Asn Gly Arg Leu Ser Cys Thr Arg Glu
    710                 715                 720

agt gat cct gta cgt gat gct gat ggc aaa tcg tac aac aat cag tgt   2263
Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr Asn Asn Gln Cys
725                 730                 735                 740
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acc atg tgt aaa gca aaa ttg gaa aga gaa gca gag aga aaa aat gag   2311
Thr Met Cys Lys Ala Lys Leu Glu Arg Glu Ala Glu Arg Lys Asn Glu
                745                 750                 755

tat tct cgc tcc aga tca aat ggg act gga tca gaa tca ggg aag gat   2359
Tyr Ser Arg Ser Arg Ser Asn Gly Thr Gly Ser Glu Ser Gly Lys Asp
            760                 765                 770

aca tgt gat gag ttt aga agc caa atg aaa aat gga aaa ctt atc tgc   2407
Thr Cys Asp Glu Phe Arg Ser Gln Met Lys Asn Gly Lys Leu Ile Cys
        775                 780                 785

act cga gaa agt gac cct gtc cgg ggt cca gat ggc aag aca cat ggt   2455
Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Lys Thr His Gly
    790                 795                 800

aat aag tgt act atg tgt aag gaa aaa ctg gaa agg gaa gca gct gaa   2503
Asn Lys Cys Thr Met Cys Lys Glu Lys Leu Glu Arg Glu Ala Ala Glu
805                 810                 815                 820

aaa aaa aag aaa gag gat gaa gac agg agc aat aca gga gaa agg agc   2551
Lys Lys Lys Lys Glu Asp Glu Asp Arg Ser Asn Thr Gly Glu Arg Ser
                825                 830                 835

aat aca gga gaa agg agc aat gac aaa gag gat ctg tgt cgt gaa ttt   2599
Asn Thr Gly Glu Arg Ser Asn Asp Lys Glu Asp Leu Cys Arg Glu Phe
            840                 845                 850

cga agc atg cag aga aat gga aag ctt atc tgc acc aga gaa aat aac   2647
Arg Ser Met Gln Arg Asn Gly Lys Leu Ile Cys Thr Arg Glu Asn Asn
        855                 860                 865

cct gtt cga ggc cca tat ggc aag atg cac atc aat aaa tgt gct atg   2695
Pro Val Arg Gly Pro Tyr Gly Lys Met His Ile Asn Lys Cys Ala Met
    870                 875                 880

tgt cag agc atc ttt gat cga gaa gct aat gaa aga aaa aag aaa gat   2743
Cys Gln Ser Ile Phe Asp Arg Glu Ala Asn Glu Arg Lys Lys Lys Asp
885                 890                 895                 900

gaa gag aaa tca agt agc aag ccc tca aat aat gca aag gat gag tgc   2791
Glu Glu Lys Ser Ser Ser Lys Pro Ser Asn Asn Ala Lys Asp Glu Cys
                905                 910                 915

agt gaa ttt cga aac tat ata agg aac aat gaa ctc atc tgc cct aga   2839
Ser Glu Phe Arg Asn Tyr Ile Arg Asn Asn Glu Leu Ile Cys Pro Arg
            920                 925                 930

gag aat gac cca gtg cac ggt gct gat gga aag ttc tat aca aac aag   2887
Glu Asn Asp Pro Val His Gly Ala Asp Gly Lys Phe Tyr Thr Asn Lys
        935                 940                 945

tgc tac atg tgc aga gct gtc ttt cta aca gaa gct ttg gaa agg gca   2935
Cys Tyr Met Cys Arg Ala Val Phe Leu Thr Glu Ala Leu Glu Arg Ala
    950                 955                 960
```

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aag ctt caa gaa aag cca tcc cat gtt aga gct tct caa gag gaa gac   2983
Lys Leu Gln Glu Lys Pro Ser His Val Arg Ala Ser Gln Glu Glu Asp
965                 970                 975                 980

agc cca gac tct ttc agt tct ctg gat tct gag atg tgc aaa gac tac   3031
Ser Pro Asp Ser Phe Ser Ser Leu Asp Ser Glu Met Cys Lys Asp Tyr
                985                 990                 995

cga gta ttg ccc agg ata ggc tat ctt tgt cca aag gat tta aag cct   3079
Arg Val Leu Pro Arg Ile Gly Tyr Leu Cys Pro Lys Asp Leu Lys Pro
           1000                1005                1010

gtc tgt ggt gac gat ggc caa acc tac aac aat cct tgc atg ctc tgt   3127
Val Cys Gly Asp Asp Gly Gln Thr Tyr Asn Asn Pro Cys Met Leu Cys
      1015                1020                1025

cat gaa aac ctg ata cgc caa aca aat aca cac atc cgc agt aca ggg   3175
His Glu Asn Leu Ile Arg Gln Thr Asn Thr His Ile Arg Ser Thr Gly
  1030                1035                1040

aag tgt gag gag agc agc acc cca gga acc acc gca gcc agc atg ccc   3223
Lys Cys Glu Glu Ser Ser Thr Pro Gly Thr Thr Ala Ala Ser Met Pro
1045                1050                1055                1060

ccg tct gac gaa tgacaggaag attgttgaaa gccatgaggg aaaaaataaa       3275
Pro Ser Asp Glu

ccccagttct gaatcaccta ccttcaccat ctgtatatac aaagaattct tcggagcttg 3335

tcttatttgc tatagaaaac aatacagagc ttttgggaat ggaatcactg attttcagtc 3395

ttttccattt ctttcctcct agaatctgtg atctgagggt ataaagacat ttccaccaag 3455

tttgagccct caaaatgtcc tgattacaat gctgtctgtc caactgcctg ttcaataaaa 3515

gtaaactcag cagaaaa                                               3532


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agtgctttttc ggccctttgt tagagatgga agacttggat gcacaaggga aaatgatcct 60
gttcttggtc ctgatgggaa gacgcatggc aataagtgtg caatg                  105


<210> 9
<211> 105
<212> DNA
<213> mammalian

<400> 9
aatgaatatc gaaagcttgt gaggaacgga aaacttgctt gcaccagaga gaacgatcct 60
atccagggcc cagatgggaa agtgcacggc aacacctgct ccatg                  105
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<210> 10
<211> 99
<212> DNA
<213> mammalian

<400> 10
cgtgaatttc gaagcatgca gagaaatgga aagcttatct gcaccagaga aaataaccct 60
gttcgaggcc catatggcaa gatgcacatc aataaatgt 99

<210> 11
<211> 105
<212> DNA
<213> mammalian

<400> 11
agtgaatttc gaaactatat aaggaacaat gaactcatct gccctagaga gaatgaccca 60
gtgcacggtg ctgatggaaa gttctataca aacaagtgct acatg 105

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<211> 156
<212> DNA
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<400> 12
aaagactacc gagtattgcc caggataggc tatctttgtc caaaggattt aaagcctgtc 60
tgtggtgacg atggccaaac ctacaacaat ccttgcatgc tctgtcatga aaacctgata 120
cgccaaacaa atacacacat ccgcagtaca gggaag 156

<211> 1064
<212> PRT
<213> Mamalia

<400> 1

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Met Lys Ile Ala Thr Val Ser Val Leu Leu Pro Leu Ala Leu Cys Leu
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Ile Gln Asp Ala Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu
             20                  25                  30

Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys
         35                  40                  45

Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala
     50                  55                  60

Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala
 65                  70                  75                  80

Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn
                 85                  90                  95

Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro
            100                 105                 110

Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn
        115                 120                 125

Arg Cys Ala Leu Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly
    130                 135                 140

Val Lys Ser Glu Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Asp Val
145                 150                 155                 160
Cys Ser Ala Phe Arg Pro Phe Val Arg Asp Gly Arg Leu Gly Cys Thr
                165                 170                 175

Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn
            180                 185                 190

Lys Cys Ala Met Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala
        195                 200                 205
Lys Arg Glu Gly Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe
    210                 215                 220

Cys Lys Glu Tyr Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr
225                 230                 235                 240

Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn
                245                 250                 255

Lys Cys Ala Leu Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu
            260                 265                 270

Asn Ser Lys Thr Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys
        275                 280                 285

Val Lys Arg Glu Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala
    290                 295                 300

Lys Asn Gly Ile Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly
305                 310                 315                 320
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Pro Asp Gly Lys Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr
                325                 330                 335

Phe Gln Ala Glu Asn Glu Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg
            340                 345                 350

Asn Lys Arg Glu Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn
        355                 360                 365

Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu
    370                 375                 380

Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys
385                 390                 395                 400

Ser Met Cys Glu Val Phe Phe Gln Ala Glu Glu Glu Glu Lys Lys Lys
                405                 410                 415

Lys Glu Gly Glu Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser
            420                 425                 430
Phe Glu Glu Leu Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg
        435                 440                 445

Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys
    450                 455                 460

Met His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Gln Glu
465                 470                 475                 480

Glu Arg Ala Arg Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys
                485                 490                 495

Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg
            500                 505                 510

Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys
        515                 520                 525
Cys Ala Met Cys Ala Ser Val Phe Lys Leu Glu Glu Glu Glu Lys Lys
    530                 535                 540

Asn Asp Lys Glu Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg
545                 550                 555                 560

Glu Ala Val Gln Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn
                565                 570                 575

Gly Arg Leu Pro Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp
            580                 585                 590

Gly Lys Ile His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln
        595                 600                 605

Gln Glu Ala Lys Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys
    610                 615                 620

Arg Glu Ala Glu Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln
625                 630                 635                 640

Asn Gly Lys Leu Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro
                645                 650                 655
```

```
Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe
            660                 665                 670

Gln Lys Glu Asn Glu Glu Arg Lys Arg Lys Glu Glu Glu Asp Gln Arg
        675                 680                 685

Asn Ala Ala Gly His Gly Ser Ser Gly Gly Gly Gly Gly Asn Thr Gln
    690                 695                 700
Asp Glu Cys Ala Glu Tyr Gln Glu Gln Met Lys Asn Gly Arg Leu Ser
705                 710                 715                 720

Cys Thr Arg Glu Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr
                725                 730                 735

Asn Asn Gln Cys Thr Met Cys Lys Ala Lys Leu Glu Arg Glu Ala Glu
            740                 745                 750

Arg Lys Asn Glu Tyr Ser Arg Ser Arg Ser Asn Gly Thr Gly Ser Glu
        755                 760                 765

Ser Gly Lys Asp Thr Cys Asp Glu Phe Arg Ser Gln Met Lys Asn Gly
    770                 775                 780

Lys Leu Ile Cys Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly
785                 790                 795                 800

Lys Thr His Gly Asn Lys Cys Thr Met Cys Lys Glu Lys Leu Glu Arg
                805                 810                 815

Glu Ala Ala Glu Lys Lys Lys Lys Glu Asp Glu Asp Arg Ser Asn Thr
            820                 825                 830

Gly Glu Arg Ser Asn Thr Gly Glu Arg Ser Asn Asp Lys Glu Asp Leu
        835                 840                 845
Cys Arg Glu Phe Arg Ser Met Gln Arg Asn Gly Lys Leu Ile Cys Thr
    850                 855                 860

Arg Glu Asn Asn Pro Val Arg Gly Pro Tyr Gly Lys Met His Ile Asn
865                 870                 875                 880

Lys Cys Ala Met Cys Gln Ser Ile Phe Asp Arg Glu Ala Asn Glu Arg
                885                 890                 895

Lys Lys Lys Asp Glu Glu Lys Ser Ser Ser Lys Pro Ser Asn Asn Ala
            900                 905                 910

Lys Asp Glu Cys Ser Glu Phe Arg Asn Tyr Ile Arg Asn Asn Glu Leu
        915                 920                 925

Ile Cys Pro Arg Glu Asn Asp Pro Val His Gly Ala Asp Gly Lys Phe
    930                 935                 940

Tyr Thr Asn Lys Cys Tyr Met Cys Arg Ala Val Phe Leu Thr Glu Ala
945                 950                 955                 960

Leu Glu Arg Ala Lys Leu Gln Glu Lys Pro Ser His Val Arg Ala Ser
                965                 970                 975
Gln Glu Glu Asp Ser Pro Asp Ser Phe Ser Ser Leu Asp Ser Glu Met
            980                 985                 990

Cys Lys Asp Tyr Arg Val Leu Pro Arg Ile Gly Tyr Leu Cys Pro Lys
        995                1000                1005
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```
Asp Leu Lys Pro Val Cys Gly Asp Asp Gly Gln Thr Tyr Asn Asn Pro
   1010                1015                1020

Cys Met Leu Cys His Glu Asn Leu Ile Arg Gln Thr Asn Thr His Ile
1025                1030                1035                1040

Arg Ser Thr Gly Lys Cys Glu Glu Ser Ser Thr Pro Gly Thr Thr Ala
                1045                1050                1055

Ala Ser Met Pro Pro Ser Asp Glu
            1060
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<400> 2

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Ser Ala Phe Arg Pro Phe Val Arg Asp Gly Arg Leu Gly Cys Thr Arg
  1               5                  10                  15

Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn Lys
             20                  25                  30

Cys Ala Met
         35
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<210> 3
<211> 35
<212> PRT
<213> Mamalia

<400> 3

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Asn Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg
  1               5                  10                  15

Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr
             20                  25                  30

Cys Ser Met
         35
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<210> 4
<211> 35
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<400> 4

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Arg Glu Phe Arg Ser Met Gln Arg Asn Gly Lys Leu Ile Cys Thr Arg
  1               5                  10                  15

Glu Asn Asn Pro Val Arg Gly Pro Tyr Gly Lys Met His Ile Asn Lys
             20                  25                  30

Cys Ala Met
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35

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<211> 35
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<213> Mamalia

<400> 5
Ser Glu Phe Arg Asn Tyr Ile Arg Asn Asn Glu Leu Ile Cys Pro Arg
1 5 10 15

Glu Asn Asp Pro Val His Gly Ala Asp Gly Lys Phe Tyr Thr Asn Lys
20 25 30

Cys Tyr Met
35

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<211> 52
<212> PRT
<213> Mamalia

<400> 6
Lys Asp Tyr Arg Val Leu Pro Arg Ile Gly Tyr Leu Cys Pro Lys Asp
1 5 10 15

Leu Lys Pro Val Cys Gly Asp Asp Gly Gln Thr Tyr Asn Asn Pro Cys
20 25 30

Met Leu Cys His Glu Asn Leu Ile Arg Gln Thr Asn Thr His Ile Arg
35 40 45

Ser Thr Gly Lys
50

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<212> DNA
<213> Mamalia

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tcaggaaatg tgccatgaat ttcaggcatt tatgaaaaat ggaaaactgt tctgtcccca 180
ggataagaaa ttttttcaaa gtcttgatgg aataatgttc atcaataaat gtgccacgtg 240
caaaatgata ctggaaaaag aagcaaaatc acagaagagg gccaggcatt tagcaagagc 300
tcccaaggct actgccccaa cagagctgaa ttgtgatgat tttaaaaaag gagaaagaga 360
tggggatttt atctgtcctg attattatga agctgtttgt ggcacagatg ggaaaacata 420
tgacaacaga tgtgcactgt gtgctgagaa tgcgaaaacc gggtcccaaa ttggtgtaaa 480
aagtgaaggg gaatgtaaga gcagtaatcc agagcaggat gtatgcagtg cttttcggcc 540
ctttgttaga gatggaagac ttggatgcac aagggaaaat gatcctgttc ttggtcctga 600
tgggaagacg catggcaata agtgtgcaat gtgtgctgag ctgtttttaa aagaagctga 660
aaatgccaag cgagagggtg aaactagaat tcgacgaaat gctgaaaagg atttttgcaa 720
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